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Abstract: BACKGROUND/AIMS To identify the number and potential causes of unnecessary diagnostic procedures in a cohort of patients with autoimmune pancreatitis (AIP). METHODS All AIP cases at our centre between April 2006 and April 2013 were collected and followed up. Diagnosis was established by the International Consensus Diagnostic Criteria (ICDC). Demographic, clinical, radiological, serological data, the number of diagnostic procedures and the reason for referral were recorded. Possible risk factors for a delayed diagnosis of AIP were analysed. RESULTS A total of 29 patients (median age 60 years; 22 males and 7 females) were diagnosed with AIP using ICDC. Twenty-five patients were diagnosed with definite, 2 with possible type 1 AIP and 2 with type 2 AIP. In 29 patients, 50 ERCPs and 18 EUS were carried out; based on ICDC recommendations, a total of 20 ERCPs and 4 EUS were unnecessary diagnostic procedures. Eight patients (23.0%) were referred for unnecessary surgery. Jaundice was shown to be a significant risk factor for unnecessary endoscopic investigations (OR 11.00, 95% CI 1.14-106.43, p = 0.04). CONCLUSION Diagnosis of AIP still remains a challenge. Patients with jaundice are at particular risk of being subjected to unnecessary endoscopic procedures. Use of ICDC would help avoid unnecessary examinations or even major surgeries at times.

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Unnecessary Procedures and Surgery in Autoimmune Pancreatitis

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Key Words
Autoimmune pancreatitis · IgG4 · IgG4-sclerosing disease

Abstract
Background/Aims: To identify the number and potential causes of unnecessary diagnostic procedures in a cohort of patients with autoimmune pancreatitis (AIP). ***Methods:*** All AIP cases at our centre between April 2006 and April 2013 were collected and followed up. Diagnosis was established by the International Consensus Diagnostic Criteria (ICDC). Demographic, clinical, radiological, serological data, the number of diagnostic procedures and the reason for referral were recorded. Possible risk factors for a delayed diagnosis of AIP were analysed. ***Results:*** A total of 29 patients (median age 60 years; 22 males and 7 females) were diagnosed with AIP using ICDC. Twenty-five patients were diagnosed with definite, 2 with possible type 1 AIP and 2 with type 2 AIP. In 29 patients, 50 ERCPs and 18 EUS were carried out; based on ICDC recommendations, a total of 20 ERCPs and 4 EUS were unnecessary diagnostic procedures. Eight patients (23.0%) were referred for unnecessary surgery. Jaundice was shown to be a significant risk factor for unnecessary endoscopic investigations (OR 11.00, 95% CI 1.14–106.43, p = 0.04). ***Conclusion:*** Diagnosis of AIP still remains a challenge. Patients with jaundice are at particular risk of being subjected to unnecessary endoscopic procedures. Use of ICDC would help avoid unnecessary examinations or even major surgeries at times.

Introduction

Autoimmune pancreatitis (AIP) is a chronic inflammatory disease of the pancreas and presents with typical clinical, radiological and histopathological characteristics. Although it is often associated with pancreatic infiltration by IgG4-positive lymphoplasmacytic cells, there are also reports of IgG4-negative AIP patients. In IgG4-positive patients with AIP, IgG4-positive lymphoplasmacytic cells are present not only in the pancreas but often additionally in other tissues. Therefore, IgG4-positive AIP is assumed to be part of an IgG4-related disease [1].

Most patients present with complaints of jaundice or abdominal pain. Less frequently, weight loss or dyspeptic symptoms are described [2–5]. The most important differential diagnosis in many cases is pancreatic cancer. In patients with AIP, symptoms of other autoimmune diseases may be apparent as well, and diabetes mellitus (DM) is frequently present (20–68%) [5]. Symptoms, however, can vary considerably. According to a large international multicenter survey, there is a wide variation especially in the distribution of jaundice and abdominal pain among patients from different parts of the world [6]. This is also the case with other organ involvement, which is reported in 15–82% of patients [6]. Diagnostic work-up is initiated mostly for unexplained symptoms of chronic pancreatitis or persistently elevated cholestatic blood values. The most typical finding on diagnostic imaging is a diffusely

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or tumour-like enlarged pancreas, with pancreatic calcification or pseudocysts seen rarely [7, 8]. Other abnormalities have been detected in imaging studies of patients with symptoms similar to those of chronic pancreatitis. In a study comparing the findings on CT of 74 patients (25 AIP, 33 pancreatic carcinoma and 16 normal pancreas), in addition to diffusely decreased enhancement of the pancreas, capsule-like rim and peripancreatic strands, pancreatic calcifications ($p = 0.04$) were more frequently detected in AIP patients and therefore were suggested as being useful for differentiating AIP from pancreatic cancer [9].

Like most autoimmune diseases, AIP responds to steroid therapy [10]. To avoid unnecessary surgery or diagnostic procedures, it is therefore important to consider the possibility of AIP at an early stage of patient work-up. Until the International Consensus Diagnostic Criteria (ICDC) for AIP (online suppl. fig. 1 and 2; for all online suppl. material, see www.karger.com/doi/10.1159/000437259) were developed, it was difficult to diagnose AIP reliably. Despite the availability of ICDC, AIP is underdiagnosed since physicians seem to be inadequately informed about them and these criteria are not routinely used in diagnosis. In order to avoid overlooking the possibility of pancreatic carcinoma which AIP mimics, diagnostic procedures and major surgery may be carried out and this might turn out to be unnecessary for this benign disease. If ICDC is used, some of these invasive procedures can be avoided. Even if cancer needs to be ruled out, once cancer work turns out to be negative, no further repeat tests should be performed.

The aim of this study, therefore, was to evaluate the delay in diagnosis of AIP and its consequences in the form of essentially unnecessary diagnostic examinations and surgical interventions due to the lack of suspicion of AIP.

Material and Methods

The study was approved by the local ethics committee (KEK-ZH-Nr.2010–0332/0).

Patients

A prospective database of patients with AIP has been maintained in our department since April 2006. Demographic data, symptoms at clinical onset, laboratory and radiological findings, as well as treatment and response to it were collected. In patients referred to our centre, patient charts were reviewed to complete data. Onset of disease was defined as the date of first AIP symptoms or the first documentation of laboratory alterations related to AIP. Presence or history of other organ involvement, laboratory findings and imaging results were recorded.

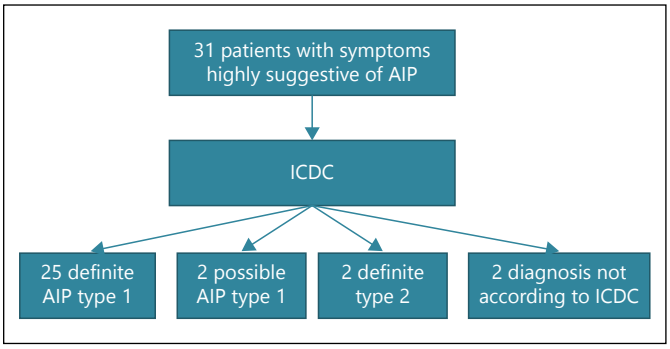

Fig. 1. Patients with symptoms highly suggestive of AIP and patients (2) not included in the study.

Definition of Required/Unnecessary Procedures

Indications for all conducted procedures like endoscopic retrograde cholangiopancreatography (ERCP) and endoscopic ultrasound (EUS) were reviewed. Based on ICDC (fig. 1 and 2; tables 1 and 2; all online suppl. material), procedures were defined as required if diagnosis could not be established as definite by histology or imaging, which then required additional work-up to exclude pancreatic carcinoma. Imaging results were also labelled as 'diffuse', 'segmental/focal' or atypical [11]. If an ERCP was conducted for the removal of a stent or drainage placed during a previous endoscopic procedure, it was labelled as required if the first procedure had been indicated. However, in those cases in which the first procedure was not indicated, the ERCP done to remove a stent or drainage also was labelled as unnecessary. Procedures were deemed unnecessary if (i) definite diagnosis of AIP was established by ICDC and no cancer work-up was required or (ii) they were repeated after their initial use yielded negative results in cancer work-up. Cancer work-up consisted of EUS with FNA if EUS showed some tumor or suspicious region in the pancreas, ERCP as well as measurement of CA 19–9.

Statistical Analysis

The Statistical Package for the Social Sciences version 20 (SPSS, Chicago, Ill., USA) was used for the statistical analysis. Crude differences with respect to unnecessary endoscopic procedures in relation to age, sex, clinical manifestation (jaundice, abdominal pain, weight loss), diabetes, other organ involvement, serology as well as imaging findings were assessed using the Fisher's exact test (Fisher's exact test used if strata comprised a sample size ≤5). A multivariate logistic regression model was calculated including only factors that were significant in the univariate analysis to identify risk factors for unnecessary endoscopic procedures.

Results

Demographic Data

A total of 29 patients with AIP (mean age 56.7 ± 19.4 years, males: 22 patients (75.9%)) were identified between April 2006 and April 2013. The mean duration of symptoms prior to diagnosis was 25.6 months. In 19 patients,

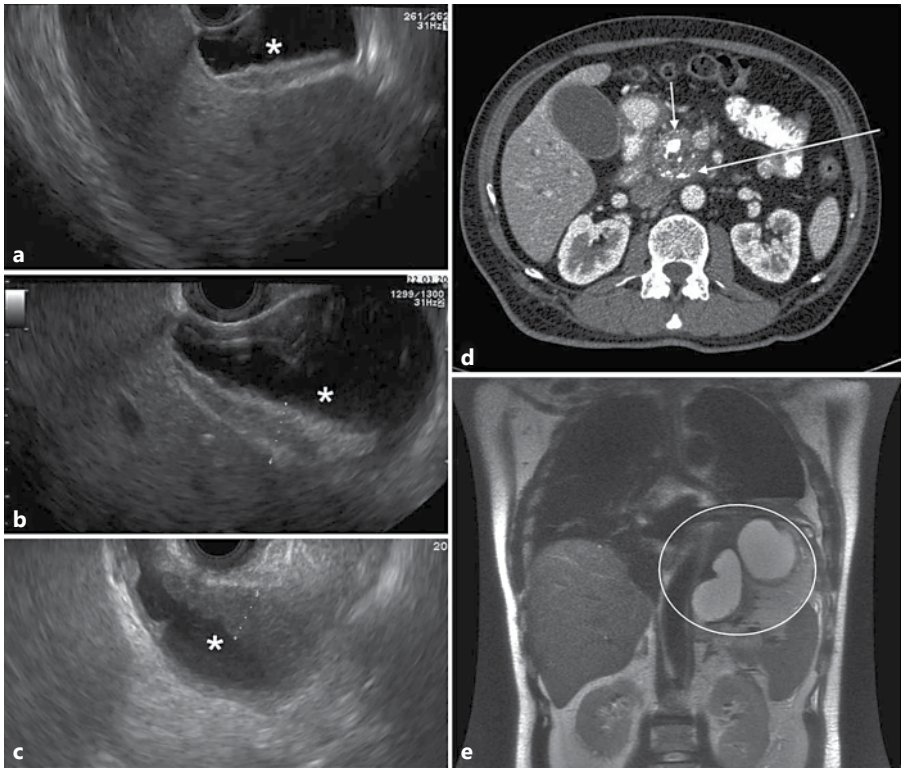

Fig. 2. Atypical imaging findings. **a**, **b** Gall bladder tumour in patient 1; **c** gall bladder tumour in patient 2; **d** pancreatic calcification; **e** pancreatic pseudocysts.

Table 1. Initial presentation of patients. Symptoms, laboratory alterations and extrapancreatic manifestations

	Cases, n	Frequency, %
Symptoms		
Abdominal pain	23	79.3
Weight loss	16	55.2
Jaundice	16	55.2
DM	11	37.9
Laboratory alterations		
Elevation of IgG4 (>upper limit of normal)	23	79.3
Elevation of IgG4 (>2 × upper limit of normal)	17	58.6
Elevation of pancreatic enzymes	14	48.3
Other organ involvement		
Biliary tree/gall bladder	14	48.3
Salivary gland	3	10.3
Orbital and lacrimal glands	3	10.3
Lymph nodes	2	6.9
Thyroid gland	1	3.4
Kidneys	1	3.4
Hypophysis	1	3.4
Skin	1	3.4
Prostate	1	3.4
Aorta	1	3.4

diagnosis was established within 6 months after onset of symptoms. The median follow-up time was 19 months (range 0–58).

Clinical Presentation

The most common symptoms at original presentation were abdominal pain (79.3%), weight loss (55.2%) and jaundice (55.2%). Out of 11 patients (37.9%) presenting additionally with DM, 7 were newly diagnosed. Two patients presented with IgG4-related disease with multiorgan involvement. One presented with infundibulohypophysitis, sicca syndrome, lymphadenopathy and prostatitis with evidence of lymphocytic infiltration, and the other with sclerosing cholangitis, thyreoiditis, DM, sicca syndrome and leukocytoclastic vasculitis. A third patient presented with AIP in combination with sclerosing cholangitis and DM and reported having had similar symptoms 27 years earlier. At that time, the patient had been diagnosed with interstitial nephritis with histological evidence of lymphoplasmacytic infiltration, which had rapidly responded to steroid therapy. Seventeen patients presented with other organ involvement (58.6%). Because an increased prevalence of inflammatory bowel disease (IBD) was reported, especially among patients with type 2 AIP, we evaluated how many of our patients had had a

Table 2. Numbers of ERCP and EUS (indicated as well as not indicated)

Patient No.	Total number of ERCP (inhouse/external)	Number of not indicated ERCP (inhouse/external)	Total number of EUS (inhouse/external)	Number of EUS done with FNA	Number of not indicated EUS (inhouse/external)
1	2 (1/1)	0	2 (1/1)	1	0
2	2 (1/1)	2 (1/1)	1 (0/1)	1	1
3	1 (1/0)	0	0	0	0
4	0	0	1 (1/0)	1	1 (1/0)
5	0	0	1 (1/0)	0	0
6	4 (1/3)	3 (1/2)	0	0	0
7	0	0	1 (1/0)	1	0
8	2 (0/2)	2 (0/2)	0	0	0
9	0	0	0	0	0
10	0	0	1 (1/0)	1	1 (1/0)
11	7 (7/0)	0	0	0	0
12	1 (0/1)	0	1 (0/1)	1	0
13	4 (0/4)	3 (0/3)	0	0	0
14	0	0	0	0	0
15	0	0	1 (1/0)	1	0
16	3 (3/0)	1 (1/0)	0	0	0
17	0	0	1 (1/0)	1	0
18	2 (0/2)	0	0	0	0
19	1 (0/1)	0	0	0	0
20	3 (3/0)	1 (1/0)	1 (1/0)	1	0
21	2 (1/1)	0	1 (1/0)	1	0
22	0	0	1 (1/0)	0	0
23	4 (0/4)	2 (0/2)	0	0	0
2006–2010	38	14	13	10	3
24	0	0	1 (1/0)	0	0
25	3 (2/1)	1 (1/0)	1 (1/0)	1	0
26	0	0	1 (1/0)	1	1
27	0	0	1 (1/0)	1	0
28	7 (7/0)	5 (5/0)	0	0	0
29	2 (1/1)	0	1 (1/0)	1	0
2011–2012	12	6	5	4	1
Total	50	20	18	14	4

colonoscopy and in how many patients diagnosis of IBD was established. In a total of 20 patients for whom data were available, it was found that colonoscopy was done among 13 patients. In 2 patients, an IBD was diagnosed. However, both patients presented with level 1 criteria for AIP type 1 and were therefore diagnosed with type 1 AIP. Data on clinical presentation and other organ involvement are shown in table 1.

Steroid Treatment and Response

Twenty seven of the 29 patients were treated with steroids (93.1%). Two patients were not treated due to prior resolution of symptoms in one and surgery in the other case. Of the 27 patients treated with steroids, 26 responded to therapy (96.3%). One patient did not respond and this is the patient who committed suicide; it was afterwards diagnosed histologically that this patient had AIP. Of the 27 patients treated with steroids, 14 experienced a relapse (51.9%).

Referrals/Diagnostic Procedures

Sixteen patients (55.2%) were referred to our centre with suspected pancreatic carcinoma, cholangiocarcinoma or carcinoma of the gallbladder (online suppl. table 3). It is of interest to note that one-fourth of patients were directly referred for surgery either because they com-

Table 3. Detailed clinical and imaging characteristics of patients, focus of ERCP

Patient No.	Year of diagnosis	Jaundice	Abdominal pain	Imaging	Imaging type of AIP	Cancer work-up indicated	Focus ERCP
1	2006	No	Yes	Indeterminate	Segmental/focal	Yes	Biliary
2	2007	Yes	Yes	Typical for AIP	Diffuse	No	Biliary
3	2007	Yes	Yes	Atypical for AIP	None	Yes	Biliary
4	2008	Yes	No	Typical for AIP	Diffuse	No	No ERCP
5	2009	No	Yes	Indeterminate	Segmental/focal	Yes	No ERCP
6	2009	Yes	Yes	Atypical for AIP	None	Yes	Biliary
7	2009	Yes	Yes	Indeterminate	Segmental/focal	Yes	No ERCP
8	2009	Yes	Yes	Typical for AIP	Diffuse	No	Biliary
9	2009	No	Yes	Atypical for AIP	None	Yes	No ERCP
10	2009	No	Yes	Typical for AIP	Diffuse	No	No ERCP
11	2009	No	Yes	Atypical for AIP	None	Yes	Pancreatic
12	2009	No	Yes	Atypical for AIP	None	Yes	Pancreatic
13	2010	Yes	No	Atypical for AIP	None	Yes	Biliary
14	2010	Yes	Yes	Typical for AIP	Diffuse	No	No ERCP
15	2010	No	Yes	Indeterminate	Segmental/focal	Yes	No ERCP
16	2010	Yes	Yes	Atypical for AIP	None	Yes	Biliary
17	2010	Yes	No	Indeterminate	Segmental/focal	Yes	No ERCP
18	2010	No	Yes	Atypical for AIP	None	Yes	Pancreatic
19	2010	Yes	No	Atypical for AIP	None	Yes	Biliary
20	2010	Yes	Yes	Atypical for AIP	None	Yes	Biliary
21	2010	Yes	No	Indeterminate	Segmental/focal	Yes	Pancreatic
22	2010	No	Yes	Atypical for AIP	None	Yes	No ERCP
23	2010	Yes	Yes	Atypical for AIP	None	Yes	Biliary
24	2011	No	Yes	Indeterminate	Segmental/focal	Yes	No ERCP
25	2011	Yes	Yes	Atypical for AIP	None	Yes	Biliary
26	2012	No	Yes	Typical for AIP	Diffuse	No	No ERCP
27	2012	No	No	Atypical for AIP	None	Yes	No ERCP
28	2012	No	Yes	Atypical for AIP	None	Yes	Biliary
29	2012	Yes	Yes	Atypical for AIP	None	Yes	Biliary

plained of chronic pain or because they were suspected to have cancer (n = 8). Only in 6 of 29 patients (20.7%), AIP has already been considered differential diagnosis before referral to our clinic. Only 3 of them had presented with typical radiological alterations. During follow-up, however, only 1 of the 29 patients of our study (3.4%) underwent surgery, due to persisting suspicion of malignant tumour, which histology revealed to be false.

In 31 patients with symptoms highly suggestive of AIP, we established the diagnosis of type 1 AIP in 27 patients and of type 2 AIP in 2 patient based on ICDC (fig. 1 and algorithm for diagnosis of AIP). In those with type 1 AIP, diagnosis was considered definite in 25 or probable in 2 patients. In the absence of the typical parenchymal finding in imaging (level 1 criterion for AIP; online suppl. tables 1–3), 23 patients required work-up for cancer who underwent a total of 46 ERCPs and 14 EUS (10 with fine needle aspiration (FNA) using a 22 gauge needle). FNA was suggestive of AIP only in 1 case; since the cancer work-up was negative, 16 of the 46 ERCPs were unnecessary. In 5 patients not requiring work-up for cancer, 4 ERCPs and 4 EUS (all of them with FNA) were performed, all of which were unnecessary. Thus, out of the 50 ERCPs and 18 EUS performed, 20 ERCPs and 4 EUS were unnecessary. In 1 patient, diagnosis could not be established using ICDC, but was established histologically after suicide. The most frequent reason for an unnecessary procedure was the placement/exchange of a drainage or stent.

Taking the year of diagnosis into account, there were 23 patients diagnosed in 2006–2010 (International diagnostic criteria were published in 2011) and 6 patients diagnosed in 2011–2012, as can be seen in tables 2 and 3. Among the 23 patients in the early study period, 38 ERCPs were performed of which 14 (36.8%) were unnecessary. Excluding 1 patient in whom 7 ERCPs were per-

Table 4. Risk factors for unnecessary endoscopic procedures in AIP patients

Variable	OR	95% CI	p value
Age older than 40	1.17	0.18–7.56	0.63
Male gender	1.17	0.18–7.56	0.63
Other organ involvement, level 1	6.50	1.05–40.13	0.03
Other organ involvement, level 2	0.50	0.48–5.24	0.50
Serology, level 1	0.66	0.13–3.19	0.45
Serology, level 2	0.86	0.13–5.56	0.63
Jaundice	9.78	1.02–93.50	0.03
Abdominal pain	1.17	0.18–7.56	0.63
Weight loss	1.02	0.21–4.98	0.65
DM	0.11	0.01–1.08	0.05
Diffuse enlargement in imaging	1.14	0.17–7.76	0.63
Focal enlargement in imaging	0.29	0.03–2.86	0.27
Pancreatic calcifications	2.83	0.45–18.04	0.26

formed due to a very complicate course of disease, there were 14 of 31 (45.1%) unnecessary ERCPs in 22 patients. Among the 6 patients diagnosed in 2011 and 2012, there were 12 ERCPs performed of which 6 (50%) were unnecessary.

There were 2 more patients likely to have had AIP. One of them was an 18-year-old girl presenting with acute pancreatitis; imaging studies showed that pseudocysts were present in the pancreatic tail even at that time. In addition, she had had abdominal pain for months before the onset of acute pancreatitis. Rapid response to treatment with prednisone together with the disappearance of the pseudocyst and abdominal pain suggest that the patient had AIP. She did not experience a relapse.

The other patient was a 66-year-old man who presented with DMs, weight loss and abdominal pain. EUS with FNA and biopsies of the papilla did not show any typical alterations for type 1 AIP. As a malignancy appeared unlikely in this setting, we started a steroid trial, to which this patient too showed good response, suggesting once again a diagnosis of AIP. However, AIP could not be established in these 2 patients using ICDC, and for this reason, they were excluded from the study.

Results of univariate analysis comparing patients with unnecessary endoscopic procedures with those without are shown in table 4. There was a significant risk for unnecessary ERCP in patients with jaundice (OR 9.78, 95% CI 1.02–93.50, p = 0.03) as well as for other organ involvement level 1 (OR 6.50, 95% CI 1.05–40.13, p = 0.03). A non-significant trend was observed for DMs (OR 0.11, 95% CI 0.01–1.08, p = 0.05).

Multivariate analysis, in which only variables with a $p \leq 0.1$, as well as age and gender were included, revealed jaundice to be a significant risk factor for unnecessary ERCP in AIP patients (OR 11.00, 95% CI 1.14–106.43, p = 0.04).

Discussion

This study with a prospective follow-up highlights the problem of diagnosing AIP. Many of our patients do not present with the classical clinical presentation of obstructive jaundice, which might be one reason why the internationally accepted diagnostic criteria are not routinely used. As shown in this study, this may lead to some unnecessary diagnostic procedures or even pancreatic surgeries and costs. Invasive endoscopic investigations such as ERCP and EUS may be necessary for ruling out malignancy if level-1 evidence for AIP, namely typical parenchymal findings, is indeterminate. However, once cancer work-up is proved to be negative, AIP should be taken into consideration. In our study, the presence of jaundice, raising the red flag of cancer, was a significant risk factor for unnecessary endoscopic procedures. There was also a trend towards an increased risk of performing additional procedures in patients with involvement of bile ducts (other organ involvement level 1), which also raises the suspicion of possible malignancy. One third of endoscopic procedures were not necessary in our AIP patients.

The two main reasons for late detection of AIP are the fear of pancreatic cancer in the presence of jaundice or a tumor like radiologic finding and the wide variety of clinical presentation of this disease entity in European patients. The typical appearance of AIP, as mainly described in the Asian literature, a sausage-like enlarged pancreas without focal lesion and jaundice was rarely present in our patients. A recent international multicentre survey by Kamisawa et al. [6] compared characteristic features of AIP in 731 Japanese, Korean, Taiwanese, Indian, US-American, German, Italian and British patients. Typical alterations in parenchyma on imaging studies, considered level-1 evidence in ICDC, are frequently missing in AIP patients. In the multicentre survey by Kamisawa et al. [6], diffuse pancreatic swelling was reported in 39–85% of Asian patients, 57% of US-American patients and 18–47% of European patients. In our study, diffuse swelling was reported in 20.7% of patients and is therefore comparable to the European data mentioned by Kamisawa et al. [6]. This finding might be due to less frequent manifestation of this phenomenon, but may also be due

to underreporting resulting from lack of knowledge of the relevance of this radiological finding to the disease and has been reported to lead to major surgery in AIP patients [12]. In case of indeterminate or even atypical imaging alterations, after excluding pancreaticobiliary cancer, clinicians have to consider AIP. Among our patients, however, there were neither typical nor indeterminate imaging alterations in 65.5% of patients. In contrast, various AIP unspecific findings such as calcifications, pseudocysts or tumour of the gall bladder (fig. 2) were found. These findings are described in patients with AIP [13], but as an initial finding it may mislead and prevent AIP suspicion.

Besides imaging, clinical and epidemiological properties of AIP differed between Asian and European patients: whereas the mean age of Asian and US-American patients varied between 59 and 66.4 years, the European patients were younger (mean age 37.5 and 57.6 years [6, 14, 15]). In our study, the mean age of patients was 56.7 years. Jaundice was the most frequent initial symptom in Asian (50–70%) and US-American patients (79%); the initial symptoms in European patients were vastly different – such as DM, weight loss, and so on. While in Italy (33%) and the United Kingdom (64%), clinical signs at onset were similarly distributed as in the United States and Asia, in Germany and in Switzerland, the most frequent clinical finding was abdominal pain in 63 and 79.3%, respectively. However, despite the diversity of clinical symptoms of AIP, not abdominal pain (present in 79.3% of our patients) but jaundice (present in 55.2% of our patients) was the risk factor for unnecessary endoscopic procedures in our study. This is most likely because jaundice led physicians to suspect the presence of pancreatic cancer.

In Asian and US-American patients, other organ involvement was reported in 33–75% of patients. Among European patients, there was an even larger variation. In the largest patient cohort from Italy (n = 87), other organ involvement was reported in 15% of patients, while in the smallest cohort from the United Kingdom (n = 28), it was 82% [6]. This, however, might be due to lack of knowledge about other organ involvement in AIP. Other organ involvement was seen in 58.6% of patients of our study.

The proportion of patients presenting with DM in our study (38.7%) is in agreement with published data. Most of the data on DM in the context of AIP, however, are from Asian countries, where rates between 20 and 68% have been described [6, 16]. In one French study, the proportion was 38.6%, while in an Italian study it was 28% [14, 17]. New-onset DM is one of the shared features of AIP and pancreatic cancer, which makes differentiating AIP from pancreatic cancer even more difficult. Here too, it would be useful to keep AIP in mind as a differential diagnosis.

Until the publication of the ICDC for AIP in April 2011 [18], no standardized universally accepted criteria for AIP were available. While in Asia the Japanese, Korean or Asian diagnostic criteria were used, the United States, India and the United Kingdom used the revised HISORt criteria, Germany used the Mannheim-Criteria and Italy the Italian criteria [17, 19–23]. These criteria varied depending on the tests for diagnosing AIP. Endoscopic retrograde pancreatogram was a central Asian criterion, while it was not included in Indian or Western criteria. Likewise, core biopsy of the pancreas was mainly included in the HISORt-criteria. In addition to providing criteria for diagnosing AIP, the ICDC also include former strategies to distinguish it from pancreatic cancer [24–26]. The ICDC are complex, but are comprehensive, since they include criteria prioritized by different countries and therefore make diagnosis of AIP possible in countries from different regions by setting up different diagnostic patterns. In our study, diagnosis of AIP could not be established by the ICDC in 1 patient, but was made by histology after the patient committed suicide. Two more patients, who we assumed had AIP because they responded to steroid therapy, were not included in the study because they failed to meet the ICDC. An under- or misdiagnosis of AIP might, however, be due to lack of knowledge of the ICDC. One major concern regarding ICDC is that typical alterations in parenchyma on imaging studies, considered level-1 evidence, are frequently missing in AIP patients. In the multicentre survey by Kamisawa et al. [6], diffuse pancreatic swelling was reported in 39–85% of Asian patients, 57% of US-American patients and 18–47% of European patients. In our study, diffuse swelling was reported in 20.7% of patients and is therefore comparable to the European data mentioned by Kamisawa et al. [6]. This finding might be due to less frequent manifestation of this phenomenon, but may also be due to underreporting resulting from lack of knowledge of the relevance of this radiological finding to the disease and has been reported to lead to major surgery in AIP patients [12]. In case of indeterminate or even atypical imaging alterations, after excluding pancreaticobiliary cancer, clinicians have to consider AIP. Among our patients, however, there were neither typical nor indeterminate imaging alterations in 65.5% of patients. There were calcifications, pseudocysts or tumour of the gall bladder (fig. 2).

The number of referrals for suspected pancreaticobiliary cancer in our study underlines the lack of knowledge of strategies to distinguish AIP from cancer. This problem was discussed by Kim et al. [27], who described that in 60% of their patients (10/17) initially a pancreatic malignancy was suspected. In another study, the pancreatic pathologies of 200 surgically treated patients with chronic pancreatitis were reviewed, of whom 53 patients were identified to have AIP. Since AIP responds to steroid treatment, correct diagnosis could have avoided surgery in these patients. Clinically suspected diagnosis leading to surgery, however, was carcinoma, carcinoma and/or chronic pancreatitis and chronic pancreatitis in 50, 2 and 1 of the 53 patients, respectively [15].

Our study had certain limitations. The first limitation was due to lack of histological evidence, and therefore, our data did not enable us to make a clear distinction between type 1 and 2 AIP in most of our patients. The 2 patients not included in the analysis might, therefore, have been type 2 AIP patients who could not be diagnosed as such due to lack of histology. Another limitation was the possibility of a referral bias. Nevertheless, we believe that our data are comparable to those from literature as reports on AIP have mainly come from other tertiary referral centres. Due to its rarity, however, it is highly likely that AIP will continue to be diagnosed at tertiary referral centres. In any case, a tertiary referral centre should be involved in the management of patients with unclear chronic or recurrent pancreatitis before being referred for surgery.

In conclusion, the features of AIP are essentially similar in Asia and the United States and are different in Europe. Besides, there is a wide diversity in the way that European patients present themselves with AIP. Therefore, diagnosis of AIP and distinguishing it from pancreatic cancer still remains a challenge. Application of the ICDC criteria should be propagated among physicians, since they enhance the possibility of early diagnosis of AIP reliably. A greater awareness of the clinical diversity of AIP and routine use of ICDC in diagnosis will enable earlier diagnosis of the disease and help avoid unnecessary diagnostic procedures and major pancreatic surgery.

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